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L15	L14	11	L15
L14	L13 with l12	11	L14
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L12	L11 with l2	637	L12
L11	plasmid	55188	L11
L10	l9 and l3	1	L10
L9	L8 with l7	10	L9
L8	linker or spacer or polylysine	330066	L8
L7	l5 with l2	540	L7
L6	L5 with l4	0	L6
L5	conjugated or complexed	113883	L5
L4	l3 with l2	14	L4
L3	NLS	1555632	L3
L2	PNA	18115	L2
L1	PNA-NLS	0	L1

END OF SEARCH HISTORY

L5 ANSWER 6 OF 6 MEDLINE DUPLICATE 1
AN 1999359788 MEDLINE
DN 99359788 PubMed ID: 10429244
TI A peptide nucleic acid-nuclear localization signal fusion that mediates nuclear transport of DNA.
AU Branden L J; Mohamed A J; Smith C I
CS Center for BioTechnology, Department of Biosciences, Karolinska Institutet, NOVUM, SE-14157, Huddinge, Sweden.. lars.branden@cbt.ki.se
SO NATURE BIOTECHNOLOGY, (1999 Aug) 17 (8) 784-7.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990916
AB We have combined a peptide nucleic acid (**PNA**) with the SV40 core nuclear localization signal (**NLS**), to create a bifunctional **PNA-NLS** peptide. The **PNA-NLS** peptide increased the nuclear uptake of oligonucleotides and enhanced the transfection efficacy of plasmids. Gene expression from an enhanced green fluorescent protein **plasmid** and a lacZ **plasmid** was preserved when hybridized to **PNA-NLS**. In combination with the transfection agent polyethyleneimine, we have improved both the nuclear translocation of fluorescence-marked oligonucleotides, and the efficacy of **plasmid** transfection, up to eightfold. The technique obviates the use of cumbersome coupling procedures of the vector due to DNA-**PNA** duplex formation or displacement of the antisense **plasmid** DNA strand by a **PNA** molecule.

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2000:441466 CAPLUS
DN 133:69802
TI Non-viral vector containing DNA encoding a therapeutic protein equipped with a nuclear localization signal peptide covalently linked to oligonucleotide (**PNA**), and its use in transfecting cells and in gene therapy
IN Behr, Jean Paul; Belguise-Valladier, Pascale; Zanta, Maria-Antonietta
PA Universite Louis Pasteur de Strasbourg, Fr.
SO Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1013770	A1	20000628	EP 1998-124578	19981223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 2000037659	A1	20000629	WO 1999-EP10281	19991222
	W: AE, AU, BG, BR, CA, CN, CZ, EE, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1141343	A1	20011010	EP 1999-966992	19991222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002533088	T2	20021008	JP 2000-589713	19991222
PRAI	EP 1998-124578	A	19981223		
	WO 1999-EP10281	W	19991222		

AB The invention provides a non-viral transfection vector comprising a DNA mol. which is delivered to the cell nucleus, whereby said DNA mol. is equipped with 1 to 15 conjugates comprising a nuclear localization signal (**NLS**) peptide linked to an oligonucleotide (peptide nucleic acid-**PNA**). The **NLS** conjugate (or **PNA**) may be covalently linked to one or both termini of a linear DNA mol., assocd. with a **plasmid** DNA mol. by forming a triple helix, or inserted in a **plasmid** DNA mol. by strand invasion. The invention also provides for the use of said non-viral transfection vector in gene therapy applications, where the DNA mol. encodes a therapeutic active protein. The invention further provides for transfection of a cell with said non-viral transfection vector. In the example section, the invention reported on the synthesis of an oligonucleotide-**NLS** peptide equipped luciferase (LUC) gene and its ligation to pCMLuc to form CMVLuc-**NLS** and showed that the **NLS** peptide allowed effective transfection with minute quantities of DNA.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2000:191243 CAPLUS
DN 132:217994
TI Transfer method using a novel synthetic transport entity for specific cellular localization of nucleic acids
IN Branden, Lars; Mohamed, Abdalla J.; Smith, C. I. Edvard
PA Karolinska Innovations A.B., Swed.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015824	A1	20000323	WO 1999-SE398	19990315
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9931784	A1	20000403	AU 1999-31784	19990315
	EP 1114172	A1	20010711	EP 1999-913793	19990315
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002525066	T2	20020813	JP 2000-570351	19990315
PRAI	SE 1998-3099	A	19980913		
	WO 1999-SE398	W	19990315		

AB The present invention relates to a novel method of genetic modification, wherein a nucleic acid of interest is transferred across a biol. membrane, and/or directed to a specific location within or on a cell, by use of a synthetic transport entity. The transport entity according to the invention is new as such and produced by coupling a functional element (FE), such as a nuclear localization signal (**NLS**), an antennapedia peptide of a protein comprising both membrane translocation and nuclear transport properties, to a binding element (BE), such as a peptide nucleic acid (**PNA**), preferably sepd. by a linker mol., which combination is then hybridized to a BE target sequence present on a carrier, which also includes the nucleic acid of interest. The present nucleic acid of interest may for example be a gene encoding a peptide, a protein or an RNA, or any other nucleic acid useful in genetic recombination events.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1999:219937 CAPLUS
DN 130:233243
TI Complexes of nucleic acid with peptide nucleic acid conjugates and their uses
IN Felgner, Philip L.; Zelphati, Oliver; Bennett, C. Frank
PA Gene Therapy Systems, Inc., USA; Isis Pharmaceuticals, Inc.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913719	A1	19990325	WO 1998-US19503	19980918
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2303908	AA	19990325	CA 1998-2303908	19980918
	AU 9895708	A1	19990405	AU 1998-95708	19980918
	EP 1014790	A1	20000705	EP 1998-949373	19980918
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001516562	T2	20011002	JP 2000-511361	19980918
	US 6165720	A	20001226	US 1998-224818	19981230
PRAI	US 1997-59215P	P	19970918		
	US 1998-87815P	P	19980529		
	US 1998-87815	A	19980529		
	WO 1998-US19503	W	19980918		

AB Complexes comprising a nucleic acid mol. and a **conjugated** peptide nucleic acid (**PNA**) are disclosed. The **PNA** may be labeled or **conjugated** to a protein, peptide, carbohydrate moiety or receptor ligand. These complexes are used to transfect cells and to monitor **plasmid** biodistribution, promote nuclear localization, induce transcriptional activation, lyse the endosomal compartment and facilitate transfection. These complexes increase the efficiency of expression of a particular gene. Thus, reporter gene-contg. **plasmid complexed** with **PNA**-rhodamine or **PNA**-fluorescein conjugates were prepd. These complexes were very stable in vitro and in vivo, they were not cleaved significantly by nucleases, and the presence of the **PNA** did not affect the biol. activity of the **plasmid**.

L7 ANSWER 7 OF 10 MEDLINE DUPLICATE 3
AN 2000419631 MEDLINE
DN 20391205 PubMed ID: 10933939
TI Targeted delivery of **plasmid** DNA to myogenic cells via transferrin-**conjugated** peptide nucleic acid.
AU Liang K W; Hoffman E P; Huang L
CS Center for Pharmacogenetics, School of Pharmacy, University of Pittsburgh, Pennsylvania 15261, USA.
NC PO1 AR 45925-01 (NIAMS)
SO MOLECULAR THERAPY, (2000 Mar) 1 (3) 236-43.
Journal code: 100890581. ISSN: 1525-0016.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000901
AB We describe a novel approach to conjugate a targeting ligand to **plasmid** DNA without affecting either its supercoiled conformation or its ability to be efficiently transcribed. A 14-mer peptide nucleic acid (**PNA**) containing lysine and cysteine on each end was designed to target to a unique sequence located at the antibiotic resistance gene of the **plasmid**. The binding of **PNA** to the **plasmid** was found to be dose-dependent and sequence-specific and not to change the conformation of the **plasmid**. Transferrin (Tf) was **conjugated** with **PNA** via a reversible disulfide bond using N-succinimidyl-3-(2-pyridyldithio)propionate. Tf-**PNA** retained the ability to the **plasmid** in a sequence-specific manner. The efficiency of this bioconjugate for delivering **plasmid** was examined in cultured myoblasts and myotubes. Naked DNA and Tf-**PNA**/DNA showed no transfection activity in either myoblasts or myotubes. Polyethyleneimine (PEI) is required for significant increase of the transfection efficiency. At N:P ratio of 5, Tf-**PNA** enhanced gene transfection about fourfold over that of the DNA/PEI complex in both myoblasts and myotubes. This enhancement could be inhibited by excess free Tf, indicating that the enhancement of transfection was through Tf-mediated endocytosis. These findings suggest that this targeting system may have the potential for gene transfer to myogenic cells in vivo.

L7 ANSWER 6 OF 10 MEDLINE DUPLICATE 2
AN 2000147366 MEDLINE
DN 20147366 PubMed ID: 10683742
TI **PNA**-dependent gene chemistry: stable coupling of peptides and oligonucleotides to **plasmid** DNA.
AU Zelphati O; Liang X; Nguyen C; Barlow S; Sheng S; Shao Z; Felgner P L
CS Gene Therapy Systems, San Diego, CA, USA.
NC 1R44CA80598 (NCI)
RR07720 (NCRR)
SO BIOTECHNIQUES, (2000 Feb) 28 (2) 304-10, 312-4, 316.
Journal code: 8306785. ISSN: 0736-6205.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000330
AB Two approaches are described for stably conjugating peptides, proteins and oligonucleotides onto **plasmid** DNA. Both methods use a peptide nucleic acid (**PNA**) clamp, which binds irreversibly and specifically to a binding site cloned into the **plasmid**. The first approach uses a biotin-**conjugated PNA** clamp that can be used to introduce functional biotin groups onto the **plasmid** to which streptavidin can bind. Atomic force microscopy images of linearized **plasmid** show streptavidin localized at the predicted **PNA** binding site on the DNA strand. Peptides and oligonucleotides containing free thiol groups were **conjugated** to maleimide streptavidin, and these streptavidin conjugates were bound to the biotin-**PNA**-labeled **plasmid**. In this way, peptides and oligonucleotides could be brought into stable association with the **plasmid**. A second approach used a maleimide-**conjugated PNA** clamp. Methods are described for conjugating thiolated peptides and oligonucleotides directly to the maleimide-**PNA**-DNA hybrid. This straightforward technology offers an easy approach to introduce functional groups onto **plasmid** DNA without disturbing its transcriptional activity.

(FILE 'HOME' ENTERED AT 18:57:50 ON 03 JAN 2003)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOTECHDS, CAPLUS' ENTERED AT 18:58:03
ON 03 JAN 2003

L1	115	S PLASMID AND PNA
L2	194545	S COMPLEXED OR CONJUGATED
L3	4186	S NLS
L4	10	S L3 AND L1
L5	6	DUP REM L4 (4 DUPLICATES REMOVED)
L6	18	S L2 AND L1
L7	10	DUP REM L6 (8 DUPLICATES REMOVED)

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